Ellen R. Westrick
Executive Director
Office of Medical/Legal
U.S. Human Health

Merck & Co., Inc.
P.O. Box 4, WP37C-116
West Point PA 19486
Tel 215 652 3476
Fax 215 652 2178

7867 '99 MAY 26 A11 :28

MERCK

May 25, 1999
(via Federal Express)

Dockets Management Branch, HFA-305
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: **Docket No. 99D-0484**
Accelerated Approval Products:
Submission of Promotional Materials

Dear Sir or Madam:

Merck & Co., Inc., supports DDMAC's effort to develop guidance regarding the submission of promotional materials to CDER and CBER for products approved under FDA's accelerated approval regulations. Having recently launched CRIXIVAN® (indinavir sulfate) as an accelerated approval product, Merck has had first-hand experience with the process and welcomes the opportunity to comment.

Merck believes that certain aspects of the draft guidance are overly restrictive in an attempt to ensure industry compliance with the requirements of 21 CFR 314.550 and 601.45, the regulations that mandate pre-clearance of promotion developed in support of accelerated approval products. While Merck supports a 30-day pre-clearance requirement for these accelerated approval materials (effective with "accelerated" marketing approval and continuing through receipt of "full" marketing approval), Merck respectfully objects to the language in the draft guidance that mandates the pre-approval submission (i.e., prior to "accelerated approval" labeling) of all materials intended for use in the initial 120 days following marketing approval of the product.

In addition to being overly restrictive, the draft guidance contradicts FDA's current recommendation that sponsors initially reach agreement with FDA on "core" documents (e.g., primary detail brochure, journal ad, announcement letters) from

99D-0484 C3

a planned launch campaign, with the understanding that additional campaign components will subsequently conform to the agreed-upon core documents. This practice reduces the *initial* volume of materials requiring DDMAC review and ensures more rapid turnaround on subsequent materials that can be prepared in compliance with core materials.

Based on our experience with CRIXIVAN, Merck believes that implementation of ongoing ("rolling") submissions can be just as effective, if not more so, in ensuring the development of appropriate promotion for accelerated approval products. It is the nature of the labeling review process for those certain products eligible for accelerated review that the text of product labeling remains in flux throughout labeling negotiations, becoming "approved product labeling" only upon receipt of final signatures to indicate Agency and sponsor agreement on all labeling issues. As described in the draft guidance, sponsors will be asked to submit draft materials intended for use during the first 120 days following marketing approval to FDA for review prior to receipt of final labeling. Merck believes this request is an inefficient use of resources at FDA and by the sponsor. Submission of materials prior to receipt of final labeling, or prior to receipt of labeling that is considered to be "close" to final labeling, practically ensures the need for extensive revisions and, therefore, subsequent agency reviews. Considering the volume of materials generally planned for use in the first 120 days following marketing approval and the number of eleventh-hour changes the labeling for products in this category may undergo, FDA demands for pre-approval submission of all materials intended for use in the first 120 days following marketing approval would place an almost impossible task on product sponsors and, at the same time, unnecessarily inflate DDMAC's workload.

In addition, as acknowledged by FDA with the inclusion of two circumstances that "may preclude a sponsor from submitting every promotional item intended for use during the 120-day post-approval period," there are important, unexpected situations that could necessitate an immediate promotional response from the sponsor (see representative list below) during the initial 120 days following marketing approval.

- Marketplace dynamics
- Patient compliance concerns
- Reprints published post-approval
- Dosing recommendations (e.g., nephrolithiasis issues with CRIXIVAN)
- Product safety issues

Merck respectfully requests that DDMAC acknowledge these exceptions not as "rare occasions" but rather as common occurrences that are impossible to predict

in the course of normal business practice. The frequency with which these unexpected situations arise could, in effect, negate any benefits expected from the pre-approval submission requirements. Merck encourages FDA to re-consider the draft guidance to address this concern.

Further, Merck is also concerned that the language of the draft guidance may be somewhat ambiguous to a sponsor with no prior exposure to the accelerated approval process. For example, the time period variously described in the draft guidance as "post-approval" and "post-marketing" could be applicable to the time period occurring pre- and post-marketing under the accelerated approval process and also to the pre- and post-marketing time periods following full approval. Clarification of the specific time period being referenced would simplify the guidance and enhance compliance.

Sincerely,

Ellen R Westrick

Ellen R. Westrick, Executive Director
Office of Medical/Legal

Federal Express®

FDA
THIS PACKAGE
HAS BEEN
X-RAYED

ELLEN WESTRICK
MERCK & COMPANY
SUMNEYTOWN PIKE
WEST POINT PA 19486
(215)652-3476

SHIP DATE: 25MAY99
ACCOUNT # 019146740
MAN-WGT:1 LBS

TO: DOCKETS MGMT. BRANCH, HFA-305
FOOD AND DRUG ADMINISTRATION
5630 FISHERS LANE, ROOM 1061
ROCKVILLE, MD 20852

( ) -

248 2802 034

FedEx. POWERSHIP 3

RELEASE#:4697309

REF: 60266.7746.010

STANDARD OVERNIGHT

WED
AA

CAD # 679410 25MAY99

Trk# 248 2802 034

FedEx Letter

IAD

20852-MD-US

ZMEDG

153077-077 RIT 7/98

The World On Time®